
=> index bioscience

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE, AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS, CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ...' ENTERED AT 09:27:57 ON 09 OCT 2008

69 FILES IN THE FILE LIST IN STNINDEX

=> ANALGESIA? OR NOCICEPTION OR PAIN OR (CHRONIC PAIN)

28374 FILE ADISCTI
2403 FILE ADISINSIGHT
11403 FILE ADISNEWS
3206 FILE AGRICOLA
125 FILE ANABSTR
385 FILE ANTE
44 FILE AQUALINE
412 FILE AQUASCI
2167 FILE BIOENG
200625 FILE BIOSIS
2129 FILE BIOTECHABS
2129 FILE BIOTECHDS
8286 FILE BIOTECHNO
16455 FILE CABA
76645 FILE CAPLUS
113 FILE CEABA-VTB
2937 FILE CIN
4664 FILE CONFSCI
2 FILE CROPB
92 FILE CROPU
6586 FILE DDFB
55789 FILE DDFU
164159 FILE DGENE
9671 FILE DISSABS
6586 FILE DRUGB
265 FILE DRUGMONOG2
81664 FILE DRUGU
3458 FILE EMBAL
380219 FILE EMBASE
50477 FILE ESBIOBASE
204 FILE FOMAD
108 FILE FOREGE
696 FILE FROSTI
285 FILE FSTA
34 FILES SEARCHED...
31231 FILE GENBANK
2314 FILE HEALSAFE
18214 FILE IIPAT
2902 FILE IMSDRUGNEWS
12587 FILE IMSPRODUCT
1717 FILE IMSRESEARCH
258 FILE KOSMET
21238 FILE LIFESCI
344075 FILE MEDLINE
1845 FILE NTIS
202 FILE NUTRACEUT
87 FILE OCEAN
127815 FILE PASCAL
16727 FILE PCTGEN
2223 FILE PHAR
2684 FILE PHARMAML

43 FILE PHIC
9083 FILE PHIN
114839 FILE PROMT
11609 FILE PROUISDDR
45 FILE RDISCLOSURE
225735 FILE SCISEARCH
36 FILE SYNTHLINE
97153 FILE TOXCENTER
42270 FILE USGENE
100315 FILE USPATFULL
7726 FILE USPATOLD
15229 FILE USPAT2
79 FILE VETB
2277 FILE VETU
76 FILE WATER
40314 FILE WPIDS
1442 FILE WPIFV
40314 FILE WPINDEX

68 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX

L1 QUE ANALGESIA? OR NOCICEPTION OR PAIN OR (CHRONIC PAIN)

=> (inhibitor or downmodulator or (slow down)) (5a) ((glutamine synthetase) or (glutamate dehydrogenase) or (pyruvate carboxylase) or (glutamine cycle) or ((glial cell) (5a)(TCA cycle)))

75 FILE AGRICOLA
2 FILE ANABSTR
2 FILE AQUALINE
30 FILE AQUASCI
49 FILE BIOENG
524 FILE BIOSIS
42 FILE BIOTECHABS
42 FILE BIOTECHDOS
12 FILES SEARCHED...
87 FILE BIOTECHNO
154 FILE CABA
598 FILE CAPLUS
17 FILE CEABA-VTB

16 FILES SEARCHED...
3 FILE CIN
4 FILE CONFSCI
2 FILE CROPB
26 FILE CROPU
5 FILE DDFB
21 FILE DDFU
104 FILE DGENE
25 FILE DISSABS
5 FILE DRUGB
26 FILES SEARCHED...

26 FILE DRUGU
1 FILE EMBAL
212 FILE EMBASE
143 FILE EMBOBASE

30 FILES SEARCHED...
3 FILE FROSTI
1 FILE FSTA
717 FILE GENBANK
50 FILE IHPAT

1 FILE IMSRESEARCH
 174 FILE LIFESCI
 236 FILE MEDLINE
 1 FILE NTIS
 2 FILE OCEAN
 134 FILE PASCAL
 47 FILES SEARCHED...
 3 FILE PHIN
 4 FILE PROMT
 7 FILE PROUSDDR
 1 FILE RDISCLOSURE
 255 FILE SCISEARCH
 194 FILE TOX CENTER
 22 FILE USGENE
 749 FILE USPATFULL
 61 FILES SEARCHED...
 162 FILE USPAT2
 2 FILE WATER
 57 FILE WPIIDS
 1 FILE WPIFV
 57 FILE WPINDEX

48 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX

L2 QUE ((INHIBITOR OR DOWNMODULATOR OR (SLOW DOWN)) (5A) ((GLUTAMINE SYNTHETAS E) OR ((GLUTAMATE DEHYDROGENASE) OR (PYRUVATE CARBOXYLASE) OR (GLUTAMIN E CYCLE) OR ((GLIAL CELL) (5A)(TCA CYCLE)))

=> (((peripheral) (5a) nervous system)) (5a) (inflammation site)
 16 FILES SEARCHED...
 30 FILES SEARCHED...
 1 FILE IFIPAT
 47 FILES SEARCHED...
 2 FILE USPATFULL
 2 FILE USPAT2
 66 FILES SEARCHED...

3 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX

L3 QUE ((PERIPHERAL) (5A) NERVOUS SYSTEM) (5A) (INFLAMMATION SITE)

=> administer? or giv? or appl? or administer or give or apply
 49180 FILE ADISCTI
 8274 FILE ADISINSIGHT
 23300 FILE ADISNEWS
 243421 FILE AGRICOLA
 142289 FILE ANABSTR
 86234 FILE ANTE
 80343 FILE AQUALINE
 189175 FILE AQUASCI
 143636 FILE BIOENG
 2139220 FILE BIOSIS
 291856 FILE BIOTECHABS
 291856 FILE BIOTECHDLS
 193567 FILE BIOTECHNO
 1143502 FILE CABA
 6195254 FILE CAPLUS
 125095 FILE CEABA-VTB

127863 FILE CIN
17 FILES SEARCHED...
57415 FILE CONFSCI
34697 FILE CROPB
137677 FILE CROPU
32779 FILE DDFB
212697 FILE DDFU
2959127 FILE DGENE
483330 FILE DISSABS
32779 FILE DRIGB
492 FILE DRUGMONOG2
437166 FILE DRUGU
16991 FILE EMBAL
1524476 FILE EMBASE
931985 FILE ESBIOBASE
29165 FILE FOMAD
4144 FILE FOREGE
136991 FILE FROSTI
165580 FILE FSTA
34 FILES SEARCHED...
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2413270 FILE IHPAT
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278 FILE IMSPRODUCT
11812 FILE IMSRESEARCH
14042 FILE KOSMET
406314 FILE LIFESCI
1652542 FILE MEDLINE
608384 FILE NTIS
2340 FILE NUTRACEUT
51729 FILE OCEAN
2020657 FILE PASCAL
22399 FILE PCTGEN
10006 FILE PHAR
21044 FILE PHARMAML
341 FILE PHIC
119793 FILE PHIN
52 FILES SEARCHED...
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8 FILE PS
18148 FILE RDISCLOSURE
2823307 FILE SCISEARCH
7267 FILE SYNTHLINE
1305970 FILE TOXCENTER
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2614212 FILE USPATOLD
709148 FILE USPAT2
3361 FILE VETB
38139 FILE VETU
128230 FILE WATER
66 FILES SEARCHED...
2919457 FILE WPIDS
33188 FILE WPIFV
2919457 FILE WPINDEX

69 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX

L4 QUE ADMINISTER? OR GIV? OR APPL? OR ADMINISTER OR GIVE OR APPLY

=> L2 and L3

11 FILES SEARCHED...
13 FILES SEARCHED...
23 FILES SEARCHED...
30 FILES SEARCHED...
44 FILES SEARCHED...
47 FILES SEARCHED...
61 FILES SEARCHED...

0 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX

L5 QUE L2 AND L3

=> L2 and L4

12 FILE AGRICOLA
3 FILE BIOENG
55 FILE BIOSIS
19 FILE BIOTECHABS
19 FILE BIOTECHDHS
12 FILES SEARCHED...
10 FILE BIOTECHNO
28 FILE CABA
75 FILE CAPLUS
17 FILES SEARCHED...
1 FILE CROPB
13 FILE CROPU
10 FILE DGENE
5 FILE DISABS
2 FILE DRUGU
1 FILE EMBAL
23 FILE EMBASE
52 FILE ESIOBASE
30 FILES SEARCHED...
2 FILE FROSTII
61 FILE GENBANK
36 FILE IFIPAT
1 FILE IMSRESEARCH
20 FILE LIFESCI
28 FILE MEDLINE
1 FILE NTIS
46 FILES SEARCHED...
25 FILE PASCAL
50 FILES SEARCHED...
1 FILE PHIN
2 FILE PROMT
1 FILE RDISCLOSURE
36 FILE SCISEARCH
35 FILE TOXCENTER
1 FILE USGENE
749 FILE USPATFULL
162 FILE USPAT2
63 FILES SEARCHED...
43 FILE WPIIDS
43 FILE WPIINDEX

34 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX

L6 QUE L2 AND L4

=> L3 and L4

13 FILES SEARCHED...
30 FILES SEARCHED...
1 FILE IIPAT...
47 FILES SEARCHED...
2 FILE USPATFULL...
2 FILE USPAT2...
65 FILES SEARCHED...

3 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX

L7 QUE L3 AND L4

=> L1 and L6

1 FILE BIOSIS...
11 FILES SEARCHED...
13 FILES SEARCHED...
3 FILE CAPLUS...
25 FILES SEARCHED...
1 FILE EMBASE...
1 FILE ESBIOBASE...
30 FILES SEARCHED...
2 FILE GENBANK...
1 FILE IIPAT...
1 FILE IMSRESEARCH...
1 FILE LIFESCI...
1 FILE MEDLINE...
44 FILES SEARCHED...
47 FILES SEARCHED...
1 FILE SCISEARCH...
2 FILE TOXCENTER...
15 FILE USPATFULL...
61 FILES SEARCHED...
4 FILE USPAT2...
1 FILE WPIDS...
1 FILE WPINDEX...

15 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX

L8 QUE L1 AND L6

=> L7 and L8

10 FILES SEARCHED...
12 FILES SEARCHED...
13 FILES SEARCHED...
23 FILES SEARCHED...
30 FILES SEARCHED...
42 FILES SEARCHED...
47 FILES SEARCHED...
59 FILES SEARCHED...
67 FILES SEARCHED...

0 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX

L9 QUE L7 AND L8

L1 and L7

12 FILES SEARCHED...
 26 FILES SEARCHED...
 35 FILES SEARCHED...
 1 FILE IFIPAT...
 47 FILES SEARCHED...
 2 FILE USPATFULL
 1 FILE USPAT2
 63 FILES SEARCHED...

3 FILES HAVE ONE OR MORE ANSWERS, 69 FILES SEARCHED IN STNINDEX

L10 QUE L1 AND L7

=> d Rank
 F1 2 USPATFULL
 F2 1 IFIPAT
 F3 1 USPAT2
 => file f1, f2, f3

FILE 'USPATFULL' ENTERED AT 10:00:40 ON 09 OCT 2008
 CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'IFIPAT' ENTERED AT 10:00:40 ON 09 OCT 2008
 COPYRIGHT (C) 2008 IFI CLAIMS(R) Patent Services (IFI)

FILE 'USPAT2' ENTERED AT 10:00:40 ON 09 OCT 2008
 CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

=> L10
 L11 4 L10
 => D L11 1-4

L11 ANSWER 1 OF 4 USPATFULL on STN
 AN 2007:88980 USPATFULL
 TI BIOINFORMATICALLY DETECTABLE GROUP OF NOVEL VACCINIA REGULATORY GENES
 AND USES THEREOF
 IN Bentwich, Itzhak, 65 Kfar Daniel, Kfar Daniel, ISRAEL 73125
 PA ROSETTA GENOMICS, Rehovot, ISRAEL (non-U.S. corporation)
 PI US 20070077553 A1 20070405
 AI US 2003-605840 A1 20031030 (10)
 DT Utility
 FS APPLICATION
 LN,CNT 126036
 INCL INCLM: 435/005.000
 INCL: 435/006.000; 536/023.720; 702/020.000
 NCL NCLM: 435/005.000
 NCL: 435/006.000; 536/023.720; 702/020.000
 IC IPC C12Q0001-70 [I,A]; C12Q0001-68 [I,A]; G06F0019-00 [I,A];
 G01N0033-48 [I,A]; G01N0033-50 [I,A]; C07H0021-04 [I,A];
 C07H0021-00 [I,C]*
 IPCR C12Q0001-70 [I,C]; C12Q0001-70 [I,A]; C07H0021-00 [I,C];
 C07H0021-04 [I,A]; C12Q0001-68 [I,C]; C12Q0001-68 [I,A];
 G01N0033-48 [I,C]; G01N0033-48 [I,A]; G01N0033-50 [I,C];
 G01N0033-50 [I,A]; G06F0019-00 [I,C]; G06F0019-00 [I,A]
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 2 OF 4 USPATFULL on STN
 AN 2007:36283 USPATFULL
 TI BIOINFORMATICALLY DETECTABLE GROUP OF NOVEL VACCINIA REGULATORY GENES

AND USES THEREOF
 IN Bentwich, Itzhak, 65 Kfar Daniel, Kfar Daniel, ISRAEL 73125
 PA ROSETTA GENOMICS, Rehovot, ISRAEL (non-U.S. corporation)
 PI US 20070031823 A1 20070208
 AI US 2003-604943 A1 20030828 (10)
 PRAI US 2003-441241P 20030117 (60)
 DT Utility
 FS APPLICATION
 LN,CNT 61464
 INCL INCLM: 435/005,000
 INCLS: 536/023,720; 702/020,000
 NCL NCLM: 435/005,000
 NCLS: 536/023,720; 702/020,000
 IC IPC1 C12Q0001-70 [I,A]; G06F0019-00 [I,A]; G01N0033-48 [I,A];
 G01N0033-50 [I,A]; C07H0021-04 [I,A]; C07H0021-00 [I,C*]
 IPCR C12Q0001-70 [I,C]; C12Q0001-70 [I,A]; C07H0021-00 [I,C];
 C07H0021-04 [I,A]; G01N0033-48 [I,C]; G01N0033-48 [I,A];
 G01N0033-50 [I,C]; G01N0033-50 [I,A]; G06F0019-00 [I,C];
 G06F0019-00 [I,A]

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 3 OF 4 IFIPAT COPYRIGHT 2008 IF on STN
 AN 04693467 IFIPAT;JFHJD;JFICDB

II Method of alleviating chronic pain via peripheral
 glutaminase regulation; Administering glutaminase inhibitor to
 a subject suffering from chronic pain at a site of
 inflammation for therapy of chronic pain

IN Miller Kenneth E
 PA Oklahoma, University of Board of Regents (61802)
 PI US 7288244 B2 20071030
 US 20030072746 A1 20030417
 AI US 2002-245094 20020913
 PRAI US 2001-318861P 20010913 (Provisional)
 FI US 7288244 20071030
 US 20030072746 20030417

DT Utility; Granted Patent - Utility, with Pre-Grant Publication

FS CHEMICAL
 GRANTED

ED Entered STN: 2 Nov 2007

Last Updated on STN: 28 Apr 2008

CLMN 16

GI 22 Drawing Sheet(s), 22 Figure(s).

FIG. 1 is a diagrammatic representation of the effects of Glutamate and glutaminase on peripheral sensory nerve stimulation and exacerbation of pain responses.

FIG. 2 is a model regarding glutamate production in primary sensory neurons during chronic inflammation. Inflammatory mediators (lightning bolts) activate and sensitize peripheral afferent terminals. This leads to the release of glutamate (GLU) and other substances from peripheral terminals causing further sensitization (arrow). Inflammation stimulates keratinocytes to increase production of nerve growth factor (NGF). NGF is taken up and retrogradely transported to the neuronal cell body where it stimulates increased production of glutaminase (GT). Increased production of GT occurs from stabilization of GT mRNA via zeta-crystallin:quinone oxidoreductase (ZC). Increased amounts of GT are shipped to the periphery causing elevated glutamate production and release, further primary afferent sensitization, and exacerbation of nociceptive responses.

FIG. 3 are photomicrographs illustrating the effects of fixation on

glutaminase (GT) immunoreactivity (IR) in the rat dorsal root ganglia (DRG). DRG sections were processed simultaneously with a mouse monoclonal GT antibody (A, C) or a rabbit polyclonal GT antiserum (B, D). Some DRG's (A,B) were fixed with 4% paraformaldehyde and others (C,D) were fixed with 70% picric acid and 0.2% paraformaldehyde. In paraformaldehyde fixed tissue, intense GT-IR was restricted to small sized DRG neurons (long arrows) with both GT antibodies (A,B). Large to medium sized neurons (short arrows) were lightly stained (A,B). In picric acid-paraformaldehyde fixed tissue, small (long arrows) and medium to large sized neurons (short arrows) contained intense GT-IR with both GT antibodies (C,D). For FIG. 4 and the data utilized to produce FIGS. 5 and 6, picric acid-paraformaldehyde fixed tissue was used with the rabbit polyclonal GT antiserum.

FIG. 4 are photomicrographs illustrating Glutaminase (GT) immunoreactivity (IR) in rat L4 dorsal root ganglia (DRG) following 7 days of CFA inflammation in the right hindpaw. DRG sections were processed simultaneously with a rabbit polyclonal GT antiserum and photographed under identical conditions. (A) In control sections, GT-IR was light to moderate in all neuronal cell sizes, small (long arrows) and medium to large (short arrows). (B) Increased GT-IR intensity was observed in small (long arrows) and medium to large neurons (short arrows) in the left (contralateral) DRG following right hindpaw inflammation. This modest increase of GT-IR was observed in the left DRG at 3 & 10 days, also. (C) Elevated GT-IR in small (long arrows) and medium to large (short arrows) neurons occurred in the right (ipsilateral) DRG following CFA inflammation of right hindpaw. This pattern also was observed at 3 & 10 days following inflammation.

FIG. 5 is a graphic illustration of an image analysis of glutaminase (GT) immunoreactivity (IR) in L4 DRG neurons after 7 days of CFA inflammation in the right paw. Data are presented as intensity divided by the area of the cell. DRG neurons were categorized into three area size groups: (A) small 100-600 μm^2 , (B) medium 600-1200 μm^2 , (C) large >1200 μm^2 . (A) Small sized neurons in the left DRG contained a significantly greater immunoreactive signal (*, $p<0.05$) than controls. Neurons in the right DRG were more intensely stained than left DRG or controls (**, $p<0.01$). (B) Medium sized neurons in the left DRG contained a significantly greater immunoreactive signal (*, $p<0.05$) than controls. Neurons in the right DRG were more intensely stained than left DRG or controls (**, $p<0.01$). (C) In the right DRG, large sized neurons were more intensely stained than the left DRG or controls (*, $p<0.05$).

FIG. 6 is a graphic illustration of GT enzyme activity in the L4 DRG at 7 days following CFA inflammation in the right hindpaw. GT activity from the right DRG (2.83 ± 0.30 moles/kg/hr) was elevated (*, $p<0.05$) over control values (2.20 ± 0.18 moles/kg/hr). The left (contralateral) L4 DRG (2.61 ± 0.20 moles/kg/hr) was not significantly different from controls or the right (ipsilateral) DRG.

FIG. 7 is a diagrammatic representation of the effects of inhibition of glutaminase on thermal and mechanical pain. The hindpaw responses to thermal stimulation (FIG. 7A) and pressure sensitivity (FIG. 7B) were determined for a control rat, a control rat following glutaminase inhibition with 6-diazo-5-oxo-L-norleucine (DON), a rat after CFA inflammation, and a rat after CFA inflammation and following glutaminase inhibition with DON.

FIG. 8A is a graphic representation illustrating the efficacy of DON to provide long term pain relief from pressure (mechanical stimulation). After administration of DON at day three following CFA inflammation, pain relief occurred for several days with three different doses of DON (0.1 10 $\mu\text{Mole}/25 \mu\text{l}$).

FIG. 8B is a graphic representation representing the DON dose response for pain relief from pressure stimulation. The area under the curve for each dose was determined from Day 3 to Day 5. No differences in the amount of pain relief were determined for the doses tested (0.1 10 mu Mole /25 mu l).

FIG. 9A is a graphic representation illustrating the efficacy of DON to provide long term pain relief to heat. After administration of DON at day three following CFA inflammation, pain relief occurred for several days with three different doses of DON (0.1 10 mu Mole /25 mu l).

FIG. 9B is a graphic representation illustrating the DON dose response for pain relief from thermal stimulation. The area under the curve for each dose was determined from Day 3 to Day 5. Pain relief was most efficacious at the higher doses (1 10 mu Mole /25 mu l).

FIG. 10 are graphic representations illustrating that intraplantar injection of DON into the hindpaw of normal rats does not affect pressure or thermal sensitivities. DON was injected (10 mu Mole /25 mu l) on day three. Both the pressure (FIG. 10A) and thermal (FIG. 10B) sensitivities in DON-treated rats were the same as saline controls.

FIG. 11A is a graphic representation demonstrating the efficacy of N-ethylmaleimide (NEM) to provide long term pain relief to pressure (mechanical stimulation). After administration of NEM (10 mM/25 mu l) at day three following CFA inflammation, pain relief occurred for several days.

FIG. 11B is a graphic representation illustrating the efficacy of NEM to provide long term pain relief from heat. After administration of NEM (10 mM/25 mu l) at day three following CFA inflammation, pain relief occurred to near normal levels at days 4 and 6.

FIG. 12 are photomicrographs illustrating glutamate immunoreactivity in tissue sections from the hindpaw skin of a control rat (FIG. 12A), a rat after CFA inflammation (FIG. 12B), and a rat after CFA inflammation and following glutaminase inhibition with NEM (FIG. 12C).

FIG. 13A is a graphic representation demonstrating the use of two inhibitors at regulatory sites on glutaminase and their efficacy to provide long term pain relief to pressure (mechanical stimulation). After administration of Palmitoyl Coenzyme A (P-CoA, 2 mM/25 mu l) or bromothymol blue (BB, 200 mu M/25 mu l) at day three following CFA inflammation, pain relief occurred for several days.

FIG. 13B is a graphic representation illustrating the efficacy of P-CoA and BB to give long term pain relief to heat. After administration of P-CoA (2 mM/25 mu l) at day three following CFA inflammation, pain relief occurred to near normal levels from Days 4 7. After BB (200 mu M/25 mu l), pain relief occurred from Days 5 7 and at near normal levels from Days 6 7.

FIG. 14 are photomicrographs illustrating that glutaminase production in many cells is regulated by zeta-crystallin:quinone oxidoreductase (ZC).

FIGS. 14A C illustrate that ZC levels are modified during chronic inflammation. ZC-immunoreactivity (IR) was examined in the rat L4 DRG during inflammation at an early and later time point (2, 6 days). ZC-IR in DRG neurons of control rats (A) shows a moderate staining of the cytoplasm of all neurons. Following inflammation for 48 hrs, ZC IR is elevated in the cytoplasm and now appears in the nuclei of many neurons (arrows). ZC IR remains elevated at 6 days of inflammation and occurs mainly in the cytoplasm although some nuclei (arrows) contain light ZC-IR.

FIG. 15 is a diagrammatic representation that illustrates that dicoumarol, a ZC inhibitor, disrupts increased glutaminase production during chronic

inflammation and decreases the prolonged hyperalgesia of chronic inflammation. Inflammation was initiated with complete Freund's adjuvant (CFA) at Day 0, and dicumarol (15 mu l @ 500 mu M) or saline was administered intrathecally on days 0, 1 and 2. Thermal latencies and pressure responses (not shown) were recorded, and both the groups with inflammation (CFA) and inflammation plus dicumarol (CFA+DC) experienced hyperalgesia and allodynia during acute inflammation (Day 1). As inflammation progressed, however, the responses of CFA+DC rats became less hyperalgesic and allodynic. At Day 3, the DRG's from the rats were collected and processed for glutaminase and ZC-IR, as shown in FIG. 16. FIG. 16 are photomicrographs illustrating that dicumarol inhibits ZC and glutaminase production. In the DRG, ZC-IR was elevated (A) in rats with inflammation, but the ZC-IR (B) from rats treated with DC during inflammation was similar to controls. ZC-IR was found in the cytoplasm and nuclei (arrows) from rats with inflammation, whereas in rats treated with DC during inflammation, the nuclei (arrows) were not stained and ZC-IR was found primarily in the cytoplasm. In the DRG, glutaminase-IR was observed at moderate levels from controls (C), elevated following inflammation (D), and similar to controls in rats treated with DC during inflammation (E).

L11 ANSWER 4 OF 4 USPAT2 on STN

AN 2003-105835 USPAT2

TI Method of alleviating chronic pain via peripheral glutaminase regulation

IN Miller, Kenneth E., Sapulpa, OK, UNITED STATES

PA The Board of Regents of the University of Oklahoma, Norman, OK, UNITED STATES (U.S. corporation)

PI US 7288246 B2 20071030

AI US 2002-245098 20020913 (10)

PRAI US 2001-318861P 20010913 (60)

DT Utility

FS GRANTED

LN,CNT 1681

INCL INCLM: 424/094,100

INCLS: 514/439,000; 514/456,000; 514/558,000; 514/561,000

NCL NCLM: 424/094,100

NCLS: 514/439,000; 514/456,000; 514/558,000; 514/561,000

IC IPCI A61K0038-43 [ICM,7]; A61K0031-385 [IC5,7]; A61K0031-353 [IC5,7]; A61K0031-352 [IC5,7,C]; A61K0031-198 [IC5,7]; A61K0031-195 [IC5,7]; A61K0031-20 [IC5,7]; A61K0031-185 [IC5,7,C*]

IPCI-2 A61K0038-43 [I,A]; A61K0031-385 [I,A]; A61K0031-353 [I,A]; A61K0031-352 [I,C*]; A61K0031-198 [I,A]; A61K0031-20 [I,A]; A61K0031-185 [I,C*]

IPCR A61K0038-43 [I,C]; A61K0038-43 [I,A]; A61K0031-00 [I,C*]; A61K0031-00 [I,A]; A61K0031-185 [I,C]; A61K0031-198 [I,A]; A61K0031-20 [I,A]; A61K0031-35 [I,C*]; A61K0031-35 [I,A]; A61K0031-352 [I,C]; A61K0031-353 [I,A]; A61K0031-385 [I,C]; A61K0031-385 [I,A]

EXF 424/94.1; 514/557; 514/561; 514/564; 514/570; 514/439; 514/456; 514/558

CAS INDEXING IS AVAILABLE FOR THIS PATENT.